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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/420,695	10/19/99	THANAVALA	Y	RPP:156A-US

HM12/1004

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EXAMINER
FLOOD,M

ART UNIT	PAPER NUMBER
1651	13

DATE MAILED: 10/04/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/420,695	Applicant(s) Thanavala et al.
	Examiner Michele Flood	Group Art Unit 1651

☒ Responsive to communication(s) filed on *Jul 19, 2000* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1 and 4-18* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1 and 4-18* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Acknowledgment is made of the receipt and entry of the amendment filed on July 19, 2000. Acknowledgment is made of Applicant's cancellation of Claims 2-3 and 19-20, and the Claims were withdrawn from further consideration by the Examiner under 37 CFR 1.142 (b).

The rejection made under 35 U.S.C. 112 has been overcome by Applicant's amendment of the claims.

The rejection made under 35 U.S.C. 102(e) has been overcome by Applicant's cancellation of Claim 19.

The provisional rejection made under 35 U.S.C. 101 has been overcome by Applicant's amendment of the claims.

Claims 1 and 4-18 are under examination.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive for the reasons below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 4-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arntzen et al. (B) in view of Koprowski et al. (A), and further in view of Stites et al. (U).

The claims are directed to a method for providing a serum IgM and IgG response specific to hepatitis B surface antigen (HBsAg) in an animal by feeding the animal or a human with a substance comprising a physiologically acceptable plant material containing HBsAg in combination with an adjuvant, the combination causing serum IgM and IgG responses specific to HBsAg in excess of serum IgM and IgG responses specific to HBsAg caused by HBsAg alone. The claims are further directed to a method wherein the plant material is from potato or tomato plant that has been genetically altered to express the antigen. The claims are further directed to a method wherein a human ingests the plant material in therapeutic dose amounts over a plurality of different times.

The rejection stands for the reasons set forth in the previous office action and repeated below.

Applicant's main argument is directed to the idea that Arntzen does not disclose or suggest the present invention and that the method for the ingestion of plant material expressing HBsAg does not give a sufficient immune response to be considered protective. Applicant further argues that Arntzen neither discloses nor suggests a way in which a high immune response could be orally obtained, that Koprowski neither teaches nor suggests any method for the oral administration of an adjuvant in combination with transgenic plant material expressing a bioactive compound for immunologic purposes, and that Stites neither teaches nor suggests that the oral administration of HBsAg in the presence of a suitable adjuvant to an animal would effect a raise in the immune response. However, this is not found persuasive because the primary reference of Arntzen was relied upon because Arntzen clearly teaches an anti-viral vaccine produced in physiologically acceptable plants, particularly the potato and the tomato, and then administered through standard vaccine procedure or by feeding the plants to an animal or a human. Arntzen specifically teaches methods of making a transgenic plant expressing an immunogen derived from hepatitis B surface antigen, wherein the immunogen is capable of eliciting an immune response in an animal by consumption of the plant material. Arntzen also teaches methods of making a vaccine by recovering the immunogen expressed in the plant cell for use as a vaccine. Moreover, Arntzen expressly teaches that the physiologically acceptable plant materials expressing the HBsAg can be used both to prime the mucosal immune system and/or stimulate the humoral immune response in a dose dependent manner. See Column 3, lines 24, Columns 4-7 and Column 8, lines 1-21. In Column 11, lines 36-50, Arntzen teaches that either the parenteral or non-

parenteral introduction of the vaccine to a mammal can elicit serum and/or secretory antibodies against the HBsAg immunogen of the vaccine with minimal induction of systemic tolerance. Finally, Arntzen teaches that a plurality of different administrations of the genetically altered plant material expressing HBsAg over separate periods of time will provide the claimed functional effect of raising the serum IgM and IgG response specific to the hepatitis B surface antigen to achieve immunization of a mammal. Note that Arntzen specifically teaches that the plurality of times for the administration of the vaccines is in a range of 3 to 6, and that the time separating the vaccinations is in a range of 14 to 35 days to achieve protective levels of antibodies. See Column 15, lines 45-61. The reference of Koprowski was primarily relied upon because Koprowski teaches a method of making transinfected plant material expressing a viral antigen which can be used as an oral delivery system to elicit an immunologic effect in an animal or human; and, the reference of Koprowski clearly teaches that when the vaccine or therapeutic compound is delivered for immunologic purposes, it could be delivered with an adjuvant to facilitate or improve its immunological therapeutical activity. See Column 6, lines 22-36. Applicant argues that Koprowski does not suggest a specific adjuvant that would have effect the instantly claimed functional effect of raising the response of serum IgM and IgG responses specific to HBsAg, however the choice of adjuvant is not commensurate with the scope of the claimed invention. The secondary reference of Stites was relied upon to demonstrate methods of providing immunological responses in an individual. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide a serum IgM and IgG

response specific to HBsAg by feeding an animal with a genetically altered plant expressing the hepatitis B surface antigen with an adjuvant, wherein the combination causes an excess of serum IgM and IgG than caused by HBsAg alone because both Arntzen and Koprowski teach that the oral delivery of genetically/and or transinfected plant material which express a viral antigen, such as the hepatitis B surface antigen taught by Koprowski, provide a positive humoral and/or mucosal immune responses when delivered to a mammal or human. At the time the invention was made, one of ordinary skill in the art would have been motivated to modify the composition of Arntzen by adding an adjuvant because Koprowski clearly teaches that the combination of plant material expressing a viral antigen and an adjuvant improves the immunological therapeutical activity of the drug. One would have been further motivated with a reasonable expectation of success because it was well known in the art as taught by Stites that adjuvants enhance the response of an immunogen when the adjuvant is administered with the immunogen. See page 102. Thus, the results are no more than the mere combination of known drugs administered by very old and well known methods in the art because Arntzen, as well as Stites, teach that protective immunity can be effected by the multiple administration of a vaccine over a period of time; and, therefore one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success that the instantly claimed method would provide the claimed functional immunological effect in an animal, wherein the animal was feed the drug combination.

As the references indicate the various proportions and amounts of the ingredients, and the plurality of times for the administration of the drugs over periods of time used in the claimed method are result variable, they would be routinely optimized by one of ordinary skill in the art practicing the inventions disclosed by each of the references.

Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

No claims are allowed.

1. **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(I). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is (703) 308-9432. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196 or the Supervisory Patent Examiner, Michael Wityshyn whose telephone number is (703) 308-4743.

mcf

September 25, 2000

LEON B. LANKFORD, JR.
PRIMARY EXAMINER